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EXAMINER	
TSAY, MARSHA M	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,648	XIAO, ZHI-CHENG	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,7,9-12,15,16,18-27 and 67-71* is/are pending in the application.

4a) Of the above claim(s) *5,7,9-11,18-27 and 68-71* is/are withdrawn from consideration.

5)☒ Claim(s) *2* is/are allowed.

6)☒ Claim(s) *12,15 and 67* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office action is in response to Applicants' after final remarks received August 13, 2007.

Prosecution on the merits of this application is reopened on claims 2, 12, 15-16, 67-71. The finality of the previous Office action is withdrawn in view of new rejections under 35 U.S.C. 112, first paragraph. The rejections are noted below.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 68-71 were inadvertently indicated to be in condition for allowance in the previous Office action. However, claims 68-71 are drawn to a method of designing a mimetic of the peptide of instant SEQ ID NO: 1. The claims are drawn to the same subject matter as claims 18-21, which were subject to restriction and withdrawn because the special technique feature is designing a peptide mimetic of instant SEQ ID NO: 1, which does not share a common special technical feature with elected Group I, now claims 2, 12, 15-16, and 67.

Accordingly, claims 68-71 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1, 3-4, 6, 8, 13-14, 17, 28-66 are canceled. Claims 5, 7, 9-11, 18-27, 68-71 are withdrawn. Claims 2, 12, 15-16, 67 are currently under examination.

Priority: The priority date is December 6, 2002.

Objections and Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 15, 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 12, 15, 67 are rejected under 35 U.S.C. 112, first paragraph, because it refers to a peptide only by function.

The court of Appeals for the Federal Circuit has recently held that such a general definition does not meet the requirements of 35 U.S.C. 112, first paragraph. "A written description of an invention involving chemical genus, like a description of a chemical species, requires a precise definition, such as be structure, formula {or} chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The court held that "in claims involving chemical materials, generic formulae usually indicate with specificity what generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish it from others. One skilled in the art therefore cannot, as one can do with a fully described genus visualize the identity of the members of the genus".

Here, the instant claims recite a peptide up to 10 amino acids in length comprising the amino acid sequence depicted as SEQ ID NO: 1. From a sequence of 10 amino acids, only seven amino acid residues are known, YLTQPQS (SEQ ID NO: 1). While Applicants have provided functional support for the peptide, there is a lack of sufficient structural information because the remaining residues in the sequence

of up to 10 amino acids have not been identified and can be selected from any of the twenty naturally occurring amino acids.

Since said products of claim 12 are inadequately described, a method of use of said products (claim 15) is also inadequately described.

The reasons are the same as noted in the previous Office action and are summarized below.

In their remarks, Applicants assert one of ordinary skill in view of the instant specification would full appreciate that the present inventors were in possession of the polypeptide encoded by SEQ ID NO: 1 and polypeptides of slightly greater length comprising this sequence (up to 10 amino acids in length). Applicants further assert that one of ordinary skill could readily identify and isolate such slightly elongated sequences based on the enabling disclosure given the requirement that the sequences must possess the "core" sequence of SEQ ID NO: 1 and bind Nogo, Nogo 66, and/or MAG. Applicants also assert that 10mers or less which do not exhibit this function are outside the scope of the present claims. Applicants' arguments have been fully considered but they are not persuasive.

Applicants have claimed an isolated peptide having up to 10 amino acids in length comprising the 7-mer sequence YLTQPQS (SEQ ID NO: 1), wherein the peptide is capable of binding to Nogo, Nogo 66, and/or MAG. If assuming a 10 amino acid long peptide, the identity of the remaining 3 amino acid residues can be selected from the 20 naturally occurring amino acids, and can even include non-natural amino acids. It is noted that Applicants are in possession of the peptide encoded by SEQ ID NO: 1. The specification discloses methods (examples 4, 5, 6) for facilitating the identification and characterization of elongated sequences comprising SEQ ID NO: 1, however, no examples of the slightly elongated sequences possessing the core sequence of SEQ ID NO: 1 are disclosed. It is known in the art that an amino acid sequence identity of 50% does not guarantee structural similarity (Yuan et al. 1998 Proteins

30: 136-143), and that even a single point mutation in a polypeptide sequence can lead to surprising alterations in protein structure and activity (Sergel et al. 2000 J Virol 74: 5101-5107).

The guidelines for the examination of patent applications under 35 U.S.C. 112, first paragraph, written description requirement, make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the genus (Federal Register Vol. 66, No. 4 pages 1099-111, January 5, 2001). As discussed above, the relevant structural features that are to be used in identifying structurally similar proteins are not well defined. In view of this, one of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of all allergen hybrid proteins. Thus, Applicants were not in possession of the polypeptides of slightly greater length comprising SEQ ID NO: 1 (up to 10 amino acids in length). Applicant is directed to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112 § 1 Written Description Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001.

Claims 12, 15, 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods and compositions of SEQ ID NO: 1 to bind to Nogo, MAG, and/or TN-F does not reasonably provide enablement for peptides up to 10 amino acids in length comprising SEQ ID NO: 1 to bind to Nogo, MAG, and/or TN-F. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which amino acid sequences, up to 10 amino acids in length, comprising SEQ ID NO: 1 will function in the same way as the wild-type peptide. Thus there could be thousands of variants which differ in sequence length and amino acid composition. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which peptides comprising SEQ ID NO: 1 were active.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since there are combinations to choose from, regarding the length and/or the specific amino acid residue. The amount of guidance in the specification is zero with regard to which and where the amino acids should be positioned as to maintain the binding activity of SEQ ID NO: 1. No working examples are present of fragments and/or differing

lengths, up to 10 amino acids in length, and/or derivative peptides of SEQ ID NO: 1. The nature of the invention is such that many different peptides that are substantially similar to SEQ ID NO: 1 may or may not have biological activity. The state of the prior art is that even peptides that are 99% similar to the wild-type peptide are at times not fully active. The relative level of skill in this art is very high. The predictability as to what substantially similar peptide will have which activity is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

Further, claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating spinal cord injury in a patient comprising injecting an effective amount of the composition of SEQ ID NO: 1 into a site of spinal cord injury does not reasonably provide enablement for a method of treating stroke damage in a patient by direct injection of an effective amount of the composition of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain the amount of SEQ ID NO: 1 that should be administered and/or the site of administration that will result in effective treatment of stroke damage. It is known in the art that although stroke is a disease of the brain, it can affect the entire body (NINDS reference sheet p. 1). The effects of stroke damage can include paralysis, one-sided weakness, problems with thinking, awareness, attention, learning, judgment, memory, numbness, in addition to understanding or forming speech (NINDS p. 1). Thus, with the many problems associated with stroke damage, it is uncertain if SEQ ID NO: 1 is enabled to treat stroke damage in a person.

In the instant case the quantity of experimentation would be large since there are many disabilities resulting from stroke damage. The amount of guidance in the specification is zero with regard to how the composition of SEQ ID NO: 1 should be administered to treat stroke damage. No working examples are present of treating stroke damage by administering SEQ ID NO: 1. The nature of the invention is such even though stroke is a disease of the brain (part of the central nervous system), it can affect the entire body. The state of the prior art is that studies are being conducted to understand stroke risk factors and the process of brain damage that results from stroke. The relative level of skill in this art is very high. The predictability as to SEQ ID NO: 1 being enabled for treating stroke damage is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

The reasons are the same as noted in the previous Office action and are summarized below.

In their remarks, Applicants assert the functional limitations recited in the claims are specific to Applicants' invention. Applicants point to the examples provided in the specification which describes the isolation and characterization of peptide sequences which bind the inhibitory domains of the myelin proteins recited in the claims. Methods for assessing the role the peptides play in CNS cells are provided in Aspect I, examples 4, 5, and 6. Applicants assert these methods facilitate the identification and characterization of peptides encompassed by the present claims. Applicants also assert that the experimentation necessary to determine the amino acids of the instant invention, up to 10 amino acids in length and including the core sequence of SEQ ID NO: 1, is merely routine and is inherent in the nature of the art. Applicants further note that several variants are disclosed in the present application and that it is well known that conservative substitutions can be made in a protein by changing the nucleic acids so that a different but similar amino acid is inserted into the polypeptide sequence. Frequently, a point mutation has no significant effect on function; therefore, one of ordinary skill can readily envisage

variants of the sequences provided that would be fully functionally but would have a slightly different sequence to the one disclosed in the application. Applicants' arguments have been fully considered but they are not persuasive.

Applicants have claimed an isolated peptide having up to 10 amino acids in length comprising the 7-mer sequence YLTQPQS (SEQ ID NO: 1), wherein the peptide is capable of binding to Nogo, Nogo 66, and/or MAG. If assuming a 10 amino acid long peptide, the identity of the remaining 7 amino acid residues can be selected from the 20 naturally occurring amino acids, and can even include non-natural amino acids. Therefore, there would be undue burden in determining the length of the peptide, in addition to selecting for the suitable amino acids. Applicants point out that examples, 4, 5, 6 provide guidance enabling one of ordinary skill to identify and characterize the peptides encompassed by the present claims without undue experimentation. However, the specification does not appear to provide clear guidance as to the structure and/or the identity of the peptides, except that it must comprise the 7-mer sequence. It is known in the art that an amino acid sequence identity of 50% does not guarantee structural similarity (Yuan et al. 1998 Proteins 30: 136-143), and that even a single point mutation in a polypeptide sequence can lead to surprising alterations in protein structure and activity (Sergel et al. 2000 J Virol 74: 5101-5107). Given that the art recognizes difficulties in identifying structurally homologous proteins and the lack of guidance in the specification concerning how one of ordinary skill is to overcome these difficulties, it does not appear that Applicants' working examples convey enablement of an isolated peptide having up to 10 amino acids in length.

Claim 16 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 2 is allowable. SEQ ID NO: 1 appears to be free of art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

August 31, 2007

M. Monshy
MARYAM MONSHIPOURI, PH.D.
PRIMARY EXAMINER